

## Systemic Adult Stem Cell Therapy for Osteoporosis-Related Vertebral Compression Fractures

### Grant Award Details

Systemic Adult Stem Cell Therapy for Osteoporosis-Related Vertebral Compression Fractures

**Grant Type:** Early Translational II

**Grant Number:** TR2-01780

**Project Objective:** To conduct POC studies for the treatment of bone fracture with homing of MSC by PTH to bone lesion. They proposed to administer human mesenchymal stem cells (MSCs) with or without concomitant administration of teriparatide (parathyroid hormone [PTH]) to treat osteoporosis related vertebral compression fractures (OVCFs).

**Investigator:**

**Name:** Dan Gazit

**Institution:** Cedars-Sinai Medical Center

**Type:** PI

**Disease Focus:** Bone or Cartilage Disease

**Human Stem Cell Use:** Adult Stem Cell

**Cell Line Generation:** Other

**Award Value:** \$1,927,698

**Status:** Closed

### Progress Reports

**Reporting Period:** Year 1

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**Reporting Period:** Year 2

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**Reporting Period:** Year 3

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## Grant Application Details

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**Application Title:** Systemic Adult Stem Cell Therapy for Osteoporosis-Related Vertebral Compression Fractures

**Public Abstract:** Vertebral compression fractures are the most common fractures associated with osteoporosis. Approximately 700,000 osteoporosis-related vertebral compression fractures (OVCFs) occur each year in the US. Currently, treatment is focused primarily on prevention. When fractures occur in patients with osteoporosis, treatment options are limited because open surgery with implants often fails. Recently, new therapies involving injection of cement into the vertebral body were developed. Unfortunately, these procedures do not regenerate bone tissue, but do incur risks of leakage and emboli. Hence, we need new treatments that directly address both the underlying cause of OVCFs (bone loss) and the inadequate repair mechanisms when fractures occur. We propose to develop a therapy that exploits mesenchymal stem cells (MSCs) stimulated in vivo with PTH (parathyroid hormone) to accelerate bone repair. PTH alone can accelerate fracture repair in healthy animals by activating bone marrow MSCs. However, osteoporotic patients have either decreased numbers of MSCs, dysfunctional MSCs, or both. In these patients, injection of MSCs combined with a PTH regimen could be an effective therapy for the treatment of multiple fractures. Our preliminary data in a mouse model demonstrated that this combined treatment enhances MSC homing to long-bone fracture sites and leads to increased repair. Here, we will build upon this foundation and ask whether a similar strategy is also effective in OVCFs. We hypothesize that PTH administration will lead to increased homing of MSCs to sites of bone fracture. We further hypothesize that PTH promotes the differentiation of MSCs into osteoblasts. Hence, our objective in the proposed study is to determine the effect of injection of MSCs combined with PTH therapy on bone regeneration in a multiple vertebral bone defect model in osteoporotic rats. The optimal doses of PTH and numbers of MSCs per injection also will be determined. Human bone marrow-derived MSCs will be injected into osteoporotic athymic rats with multiple lumbar vertebral bone defects. MSC homing to bone defects will be monitored using micro- and molecular imaging. Subsequent studies will test increasing dosages of PTH to define the optimal dose for maximal enhancement of MSC homing to a fracture. Bone regeneration will be monitored using micro-CT imaging and biomechanical analyses (to determine structural integrity of newly repaired bone). Subsequent studies will determine whether increasing the number of injected MSCs linearly enhances bone tissue formation. These studies will aid in the creation of an evidence base for future clinical trials that could revolutionize the treatment of vertebral fractures and other complex fractures in patients suffering from osteoporosis.

**Statement of Benefit to California:**

Approximately 10 million people in the United States are diagnosed as osteoporotic, while an additional 34 million are classified as having low bone mass. The lifetime incidence of fragility fractures secondary to osteoporosis in females over fifty years of age is approximately 1 in 2, and in males over the age of fifty, is 1 in 4. Osteoporosis-related vertebral compression fractures (OVCFs) are the most common fragility fractures in the United States, accounting for approximately 700,000 injuries per year, twice the rate of hip fractures. Approximately 70,000 OVCFs result in hospitalization each year with an average hospital stay per patient of 8 days. Fragility fractures due to osteoporosis also place a severe financial strain upon the health care industry. Estimates show there were approximately 1.5 million osteoporosis-related fractures in the United States in 2001, the care of which cost about \$17 billion. Moreover, as the number of individuals over the age of fifty continues to increase, costs are predicted to rise to an estimated \$60 billion a year by the year 2030. OVCFs have previously received limited attention from the spine care community. This oversight may be a result of the perception that OVCFs are benign, self-limited problems or that treatment options are limited. However, it has become clear that OVCFs are associated with significant physiologic and functional impairment, even in patients not presenting for medical evaluation at the time of fracture. Current treatment of osteoporotic patients is mostly focused on prevention of OVCFs. There are a few options of treatment when OVCFs actually occur. Since open surgery involves morbidity and implant failure in the osteoporotic patient population, nonoperative management, including medications and bracing, is usually recommended for the vast majority of patients. Unfortunately, large numbers of patients report intractable pain and inability to return to activities. Currently there is no efficient biological solution for the treatment of OVCFs. The proposed study will further develop a biological therapeutic solution that will accelerate repair of OVCFs. The treatment will rely upon a combination of drug and adult stem cell therapy; both are either approved for clinical use or in clinical trials. It will also involve a simple intravenous injection instead of a percutaneous injection of a polymer, which does not restore lost bone tissue. Data generated from this study could potentially revolutionize the treatment of vertebral fractures and other complex fractures in patients suffering from osteoporosis, and so benefit the citizens of California by reducing hospitalization periods, operative costs and loss of workdays, and by improving quality of life for Californians with osteoporosis that are at risk for OVCFs.

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